NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 58 draft remits and draft scopes and Summary of comments and discussions at scoping workshops

Topic ID	Topic title
1303	Tezacaftor and ivacaftor combination therapy for treating cystic fibrosis with the F508del mutation
1211	Cannabidiol for adjuvant treatment of seizures associated with Dravet syndrome or Lennox-Gastaut syndrome
877	Patiromer for treating hyperkalaemia
1213	Dupilumab for treating uncontrolled asthma
1293	Sodium zirconium cyclosilicate for treating hyperkalaemia
1050	NBTXR-3 for treating soft tissue sarcoma

Provisional Title	Tezacaftor and ivacaftor combination therapy for treating cystic fibrosis with the F508del mutation		
Topic Selection ID Number	8423	**Wave / Round**	194
TA ID Number	ID 1303		
Company	Vertex Pharmaceuticals		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of tezacaftor in combination with ivacaftor within its marketing authorisation for treating cystic fibrosis in people with the F508del mutation		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of tezacaftor and ivacaftor for treating cystic fibrosis is appropriate. The proposed remit is appropriate. No changes are required. The company commented that the STA process is not an adequate mechanism to assess precision medicines for small patient populations / orphan diseases. Lumacaftor-ivacaftor was appraised as an STA primarily because of the population size. The anticipated indication for tezacaftor-ivacaftor is broader than that for lumacaftor-ivacaftor, covering a bigger population. The topic selection group agreed that the STA process was appropriate.		
Population size	Cystic Fibrosis Trust: Around **8671** people in the UK have CF with at least one F508del mutation. • Of these, **4789 (50.2%)** are homozygous for the F508del mutation and **3882 (40.7%)** are heterozygous for the F508del mutation. • Not all heterozygous patients are included in the anticipated licence. Therefore the number of people eligible for tezacaftor/ivacaftor will be less than **8700**, but greater than **5000**		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	Unknown; he cost of tezacaftor with ivacaftor is not yet known.		
Timeliness statement	***CONFIDENTIAL INFORMATION REMOVED***publication of timely guidance will not be possible.		

Provisional Title	Cannabidiol for adjuvant treatment of seizures associated with Dravet syndrome or Lennox-Gastaut syndrome		
Topic Selection ID Number	8469	**Wave / Round**	202
TA ID Number	ID 1211		
Company	GW Pharmaceuticals		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of cannabidiol within its marketing authorisation for adjuvant treatment of seizures associated with Dravet syndrome or Lennox-Gastaut syndrome.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of cannabidiol for treating Dravet syndrome or Lennox-Gastaut syndrome is appropriate. The proposed remit is appropriate. No changes are required. This was scoped as a single STA. However comments from stakeholders suggests that although there are similarities between the 2 conditions, there are differences in the populations and clinical management that would make a single STA complex and inappropriate. In addition, the company highlighted the possibility of the EMA granting separate marketing authorisations rather than a single licence as expected. The topic selection group agreed that the proposed remit remains relevant for either scenario. Therefore it agreed to proceed with the current remit, with the possibility of splitting the appraisal into 2 STAs after referral.		
Population size	The prevalent population in England: • Dravet syndrome - between 1,350 and 2,700 • Lennox-Gastaut syndrome - around 5000 No data on the number of people who would be considered to be inadequately controlled by anti-epileptic drugs. • Both these conditions are known to be drug resistant, and the clinical experts at the scoping workshop considered the proportion eligible for this treatment to be relatively high.		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	Unknown; the cost of cannabidiol is not yet known. There may be offsetting savings from people transferring from alternative treatment options, but the new technology may be used in addition to current treatment options in which case all costs will be incremental.		

Timeliness statement	Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible.

Provisional Title	Patiromer for treating hyperkalaemia		
Topic Selection ID Number	7866	**Wave / Round**	
TA ID Number	877		
Company	Vifor Fresenius Medical Care Renal Pharma UK		
Anticipated licensing information	Marketing authorisation: Patiromer received its marketing authorization on 19 July 2017. Wording of marketing authorisation: 'Patiromer is indicated for the treatment of hyperkalaemia in adults'		
Draft remit	To appraise the clinical and cost effectiveness of patiromer within its marketing authorisation for treating hyperkalaemia.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of patiromer for treating hyperkalemia is <u>appropriate</u>. The proposed remit is appropriate. No changes are required. Attendees at the scoping workshop discussed how patiromer will be used in clinical practice. The population and comparators in the scope have been amended consistent with the expected use of patiromer. Minor changes have also been made to the outcomes and subgroups. Consultees also discussed whether a MTA which included patiromer and sodium zirconium cyclosilicate (ZS-9) was appropriate. They noted that although ZS-9 may get a marketing authorisation similar to patiromer, it would have a broader clinical use including treatment of acute severe hyperkalemia. They agreed that an MTA would not be appropriate, given the differences in the expected use of the two technologies.		
Population size	Less than 250,000 people in England would be eligible for treatment with this technology. Estimate calculations: • No of people (16 or over) with CKD stage 3-5: 2.6 million (6.1% of the population) • No. of people receiving renal-replacement therapy (CKD stage 5) and would not require patiromer: 48,000=0.48 million • No of people with CKD stage 3 and 4= 2.60 -0.48=2.12 million • Prevalence of CHF= 434,904 Estimated overlap: • CKD is present in 35—70% of CHF patients (average: 52.5%) • No of people with CHF who don't have CKD 434,904* (1-0.525)= 206,579 • Total population=2,120,000 + 206,579= 2,326,579 • Most of them would receive RAASi Incidence of hyperkalemia with RAASi use in patients with CKD or heart failure: ~5%-10%= 116,329 to 232,658		

Process (TA/HST)	TA
Proposed changes to remit (in bold)	None
Costing implications	Unknown; the cost of patiromer is not yet known. The duration of the treatment has not been provided. Therefore the resource impact cannot be estimated at this stage, but based on the size of the population may be substantial.
Timeliness statement	Considering that this product has received a marketing authorisation for use in the UK, publication of timely guidance will not be possible.

Provisional Title	Dupilumab for treating uncontrolled asthma		
Topic Selection ID Number	8615	**Wave / Round**	207
TA ID Number	1213		
Company	Sanofi		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of dupilumab within its marketing authorisation for treating severe asthma inadequately controlled with inhaled corticosteroids.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of dupilimab for treating uncontrolled asthma is <u>appropriate.</u> The proposed remit is not appropriate and should be amended as follows: to appraise the clinical and cost effectiveness of dupilumab within its marketing authorisation for treating **moderate to** severe asthma inadequately controlled with **optimised standard therapy**. The remit has been updated because dupilimuab is likely to get a marketing authorisation in moderate and severe disease, and add on to 'optimised standard therapy' is broader than people with uncontrolled asthma on ICS. Dupilumab is intended to be used at stage IV/V of the GINA pathway (this includes people with severe asthma taking oral corticosteroids) whereas people inadequately controlled on ICS are earlier than this. The attendees of the workshop discussed the likely use of dupilumab in the treatment pathway. Dupilumab is intended to treat people with type 2 asthma involving IL5 overproduction. Type 2 asthma includes people with IgE-mediated allergic asthma and/or eosinophilic asthma but may also include people with neither IgE mediated allergic or eosinophilic asthma. The scope has therefore been updated to include comparators for IgE mediated allergic asthma (omalizumab) and eosinophic asthma (reslizumab, mepolizumab and potentially benralizumab).		
Population size	Approximately 7500 people in England would be eligible for treatment with dupilumab. The difficult asthma registry states that 5.4 million people in the UK are currently receiving treatment for asthma (1.1 million children (1 in 11) and 4.3 million adults (1 in 12). This consists of 932,000 children and 3,600,000 adults. The registry also reports that approximately 5-10% of would have difficult to treat asthma which would equate to 270,000 – 540,000 people. The scoping workshop report for mepolizumab for treating severe eosinophilic asthma states that "severe difficult to control asthma has an estimated prevalence of 140 patients/million population. In England with a population of 53.9 million there are approximately 7546 people with severe difficult to control asthma.		

Process (TA/HST)	TA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of dupilumab within its marketing authorisation for treating **moderate to** severe asthma inadequately controlled with ~~inhaled corticosteroids~~ **optimised standard therapy**.
Costing implications	Although the actual dosing and unit cost may be different, based on a list price of £1264.89 for 300mg/2ml solution and a dose of 300mg every 2 weeks, the annual cost per patient would be around £32,900. Offsetting savings are likely as a result of stopping/replacing other treatment options.
Timeliness statement	Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible.

Provisional Title	Sodium zirconium cyclosilicate for treating hyperkalaemia		
Topic Selection ID Number	7722	**Wave / Round**	139
TA ID Number	1293		
Company	AstraZeneca		
Anticipated licensing information	CHMP positive opinion was received February 2017 but was under review. In January 2018 the CHMP confirmed the positive opinion and recommended the granting of a marketing authorisation for the treatment of hyperkalaemia in adult patients. ***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of sodium zirconium cyclosilicate within its marketing authorisation for treating hyperkalaemia.		
Main points from consultation	Scope consultation to be completed. During the consultation and scoping workshop for the draft scope for patiromer for treating hyperkalaemia, NICE invited comments on the appropriateness of a multiple technology appraisal (MTA) that included both patiromer and sodium zirconium cyclosilicate (ZS-9). Stakeholders commented that although ZS-9 may receive a marketing authorisation similar to patiromer, it would have a broader clinical use including treatment of both acute and chronic hyperkalemia. The attendees agreed that an MTA would not be appropriate, given the differences in the expected use of the two technologies.		
Population size	It is likely that the population size will be similar to that estimated for patiromer for treating hyperkalaemia – estimate and calculations noted below; Fewer than 250,000 people in England would be eligible for treatment with this technology. Estimate calculations: • No of people (16 or over) with CKD stage 3-5: 2.6 million (6.1% of the population) • No. of people receiving renal-replacement therapy (CKD stage 5) and would not require patiromer: 48,000=0.48 million • No of people with CKD stage 3 and 4= 2.60 -0.48=2.12 million • Prevalence of CHF= 434,904 • Estimated overlap: • CKD is present in 35—70% of CHF patients (average: 52.5%) • No of people with CHF who don't have CKD 434,904* (1-0.525)= 206,579 • Total population=2,120,000 + 206,579= 2,326,579 • Most of would receive RAASi • Incidence of hyperkalemia with RAASi use in patients with CKD or heart failure: ~5%-10%= 116,329 to 232,658		

Process (TA/HST)	TA
Proposed changes to remit (in bold)	None
Costing implications	There were 7,000 hospital admissions for hyperlakaemia in 2013/14 however, the total number of people in England with hyperlakaemia is unknown. Sodium zirconium cyclosilicate is administered orally and its cost is unknown.
Timeliness statement	Based on current information on the anticipated date of marketing authorisation, the opportunity to publish timely guidance for this topic is unlikely. This topic was previously B-listed at topic selection but reconsidered following challenge from the company. The company has advised that the topic should be scheduled in line with the estimated launch date due to uncertainty about the date of the marketing authorisation. Using the anticipated launch date as the driver for guidance publication (instead of the marketing authorisation) would enable NICE to publish 'timely' guidance.

Provisional Title	NBTXR-3 for treating soft tissue sarcoma		
Topic Selection ID Number	8247	**Wave / Round**	
TA ID Number	1050		
Company	Nanobiotix		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***Expected wording: NBTXR-3 is indicated for treating soft tissue sarcoma		
Draft remit	To appraise the clinical and cost effectiveness of NBTXR-3 within its CE marked indication for neoadjuvant treatment of soft tissue sarcoma		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of NBTXR-3 for treating soft tissue sarcoma is <u>appropriate</u> The proposed remit is appropriate. No changes are required. A scoping workshop was organised because NBTXR-3 is a type of device that hasn't been appraised by NICE before and it is the first appraisal of a neoadjuvant treatment for soft tissue sarcoma. The workshop was subsequently cancelled as there was only one consultation response received from Sarcoma UK. A clinical expert specialising in treating soft tissue sarcoma was contacted by NICE. The clinical expert considered this appraisal to be appropriate because it could improve outcomes for patients (increase the likelihood of successful surgery with lower local recurrence).		
Population size	Fewer than **2,000** people in England would be eligible for treatment with NBTXR-3. The population in the clinical trial of NBTXR-3 for sarcoma is narrower than the population the company states its marketing authorisation will cover. The population estimate is based on the population eligible for NBTXR-3 in the trial • soft tissue sarcoma (UK): 3,330 (this includes people with GIST, gastrointestinal stromal tumours) • Proportion of people with extremity or trunk soft tissue sarcoma 60% = 1,998 • Proportion who are a candidate for preoperative radiotherapy (unresectable tumour or unfeasible carcinological surgery). Itis unclear therefore the proportion of patients who may be eligible for treatment..		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	The likely population could not be determined and the unit cost for NBTXR-3 is not yet known so the resource impact of this		

	technology could not be estimated There may be offsetting savings for people transferring from the current treatment options.
Timeliness statement	***CONFIDENTIAL INFORMATION REMOVED***publication of timely guidance will not be possible.